EVENT ABSTRACT

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Investigation of Dendrimer-based nanoparticles cellular uptake and cell tracking in a semi-automated microfluidic platform

Mariana Carvalho[1, 2*], Fátima R. Maia[1, 2], Rui L. Reis[1, 2*] and Joaquim M. Oliveira[1, 2*]

[1] University of Minho, 3B's Research Group - Biomaterials, Biodegradables and Biomimetics, Portugal

[2] PT Government Associate Laboratory, ICVS/3B's, Portugal

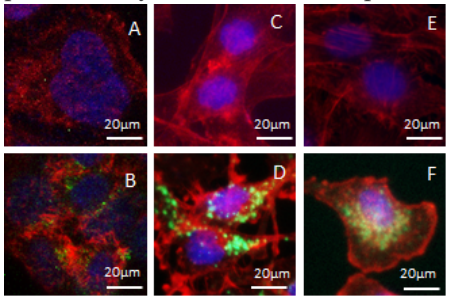
Introduction: A microfluidic device such as Kima Pump and Vena8 biochip is able to realize functions that are not easily imaginable in conventional biological analysis, such as highly parallel, sophisticated high-throughput analysis and single-cell analysis in a well-defined manner [1].

Cancer cell tracking within the microfluidic model will be achieved by grafting fluorescent label probe Fluorescein-5(6)-isothiocyanate (FITC) to dendrimer nanoparticles allowing cell visualization by immunofluorescent staining followed by fluorescence microscopy. In this study, synthesis and physicochemical characterization of Carboxymethyl-chitosan/poly(amidoamine) dendrimer nanoparticles (CMCht/PAMAM NP's) were performed[2]. Several cancer cell lines such as a HeLA (cervical carcinoma cell line), HTTC-116 (Colon Carcinoma) and Glioblastome cell line (GBM) were exposed to different concentrations of CMCht/PAMAM dendrimer nanoparticles over a period of 7d. After finding the adequate NP concentration, the internalization efficiency was tested, as well as cellular trafficking, in static and dynamic conditions (Kima Pump bioreactor).

Experimental Methods: CMCht/PAMAM NP's were synthetized and labelled with fluorescein isothiocyanate (FITC) according to Oliveira et al.[3]

To access internalization efficiency, semi-automated microfluidic platform, Vena8 Endothelial+ biochips (Cellix®, Dublin, Ireland) was used to mimic physiological flow conditions. Biochips were coated using a standard pipette tip and ~12 µL of fibronectin (Sigma, Germany) into each microchannel and placed at 4ºC for overnight coating, followed by cell seeding. A solution of FITC-CMCht/PAMAM NP's at a concentration of 0.4 mg.mL-1 was prepared in a complete culture medium and then transferred to Kima Pump. Perfusion was performed for 24 hrs and 48 hrs at a flow rate of 2 µL/min for 2 min. (Period I) followed by 20 min of pause (Period II).

Results and Discussion: CMCht/PAMAM NP's were successfully synthetized as shown by H1NMR analyses. Moreover, they exhibited good physicochemical properties, with a consistent nanosphere-like shape and a diameter of ~30 nm, as shown by TEM, DLS and AFM analysis. Fluorescent-probe labelled CMCht/PAMAM NP's were found to be internalized with high efficiency by all cell types, either in conventional static conditions and when seeded and grown in a biochip under perfusion with Kima Pump. It was found that the best flow rate was 2 µL/min (Period I), followed by a pause of 20 min. (Period II). Kima Pump bioreactor permits reaching cell confluence in dynamic conditions in just 3 hours and allows the assay to start promptly consisting in a faster way to perform assays with lower consumption of reagents and materials.



Conclusion: CMCht/PAMAM NP's were successfully synthetized. Fluorescent probe labelled nanoparticles were found to be internalized with high efficiency in several cancer cell lines, either in conventional static conditions and when seeded and grown in a biochip under perfusion with Kima Pump. It is our particular interest to engineer the CMCht/PAMAM NPs for applications in the intracellular controlled delivery of biological agents, cell tracking and differentiation, together with the optimization of the bioreactor and biochips to create new models of disease.

The future of this work is to develop a microfluidic chip-based 3D cell culture system for cancer research, using several cancer cell types and different biomaterials as 3D ECM.

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*** Correspondence:**
Dr. Mariana Carvalho, University of Minho, 3B's Research Group - Biomaterials, Biodegradables and Biomimetics, Guimarães, Portugal, Email1
Dr. Rui L Reis, University of Minho, 3B's Research Group - Biomaterials, Biodegradables and Biomimetics, Guimarães, Portugal, rgreis@dep.uminho.pt
Dr. Joaquim M Oliveira, University of Minho, 3B's Research Group - Biomaterials, Biodegradables and Biomimetics, Guimarães, Portugal, miguel.oliveira@dep.uminho.pt